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EXAMINER	
1641	
ART UNIT	PAPER NUMBER
	20

DATE MAILED: 05/08/98

Below is a communication from the EXAMINER in charge of this application

COMMISSIONER OF PATENTS AND TRADEMARKS

ADVISORY ACTION

☒ THE PERIOD FOR RESPONSE:

a) ☒ is extended to run 4 months or continues to run _____ from the date of the final rejection

b) ☐ expires three months from the date of the final rejection or as of the mailing date of this Advisory Action, whichever is later. In no event however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition , and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

☐ Appellant's Brief is due in accordance with 37 CFR 1.192(a).

☒ Applicant's response to the final rejection, filed 4/27/98 has been considered with the following effect, but it is not deemed to place the application in condition for allowance:

1. ☒ The proposed amendments to the claim and /or specification will not be entered and the final rejection stands because:

   a. ☐ There is no convincing showing under 37 CFR 1.116(b) why the proposed amendment is necessary and was not earlier presented.

   b. ☒ They raise new issues that would require further consideration and/or search. (See Note).

   c. ☒ They raise the issue of new matter. (See Note).

   d. ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

   e. ☐ They present additional claims without cancelling a corresponding number of finally rejected claims.

   NOTE: See attached

2. ☐ Newly proposed or amended claims _____ would be allowed if submitted in a separately filed amendment cancelling the non-allowable claims.

3. ☒ Upon the filing an appeal, the proposed amendment ☐ will be entered ☒ will not be entered and the status of the claims will be as follows:

   Claims allowed: None
   Claims objected to: None
   Claims rejected: 1-4, 8-14, 16, 20, 23, 24, 27-29, 37

   However;

   ☐ Applicant's response has overcome the following rejection(s): _____

4. ☒ The ~~affidavit, exhibit or~~ request for reconsideration has been considered but does not overcome the rejection because See Attached

5. ☐ The affidavit or exhibit will not be considered because applicant has not shown good and sufficent reasons why it was not earlier presented.

☐ The proposed drawing correction ☐ has ☐ has not been approved by the examiner.

☐ Other

DETAILED ACTION

The Group and/or Art Unit location of your application in the Patent and Trademark Office has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1641. This change is effective as of February 7, 1998.

The Examiner acknowledges receipt of the Amendment After Final filed April 27, 1998.

The text of those sections of U.S. Code not included in this Office Action can be found in a prior Office Action.

Response to Amendment

The amendment filed April 27, 1998 under 35 CFR 1.116 in response to the final rejection has been considered but is not deemed to place the application in condition for allowance and will not be entered because: the newly added claim 39 recites the limitation "the essential gene does not encode a trans regulatory element for the lethal gene". This limitation is viewed as new matter as it does not appear to be supported by the specification as originally filed. Since the new claim raises new issues and

would require further consideration and/or search, Applicant's Amendment After Final will not be entered and the claims stand as recited in the previous Office Action.

(1) The rejection of claims 1-4, 8-14, 16, 20, 23, 24, 27-29, and 37 under 35 U.S.C. 112, first paragraph is maintained.

(2) The rejection of claims 1-3, 10-13, 16, 20, 23, 24, 27, 28, and 37 under 35 U.S.C. 102(b) as being anticipated by Gerdes et al (Proc. Natl. Acad. Sci.) is maintained.

(3) The rejection of claims 1-3, 8, 10-14, 16, 20, 27, 28, and 37 under 35 U.S.C. 102(b) as being anticipated by Gerdes et al (EMBO Journal) is maintained.

Applicant's arguments filed September 18, 1997 have been fully and carefully considered and they are not deemed to be persuasive regarding those rejections which are maintained.

(a) In response to the rejection of claims 1-4, 8-14, 16, 20, 23, 24, 27-29, and 37 under 35 U.S.C. 112, first paragraph, Applicant submits that the claimed "Environmentally Limited Viability System (i.e. the regulated essential and lethal genes recited in the claims) is **not** a bacterial attenuation system. Rather, the environmentally regulated expression of the lethal and essential

genes results in cell **viability** in the permissive environment and cell **non-viability** in the non-permissive environment."

It is the Examiner's position that the claims are directed to "an isolated microbial cell comprising an Environmentally Limited Viability System". In addition, the claims indicate that the cell is viable in a permissive environment (e.g., inside a warm-blooded animal). The claims, therefore, can be interpreted as administering live virulent microorganisms to an animal host. The specification does not teach how to administer live virulent microorganisms as a vaccine composition, or whether such a composition would provide protection. Furthermore, the specification teaches that any bacteria can serve as the host for the Environmentally Limited Viability System. However, the specification does not teach how to use bacteria such as *Yersinia pestis* or *Moraxella catarrahalis*, for example, as vaccine compositions. Although the specification teaches that some examples are "vaccines for the control of plague caused by *Yersinia pestis*, of gonorrhea caused by *Neisseria gonorrhoea*, of syphilis caused by *Treponema pallidum*" (see page 36, lines 25-27), there are no known vaccines for these diseases. Although the specification provides some general guidance with respect to how to use the composition, there are no working examples. In

view of the absence of working examples, the breadth of the claims, and the unpredictable state of the art, it would require undue experimentation for one skilled in the art to practice the entire scope of the claimed invention.

(b) In response to the rejection of claims 1-3, 10-13, 16, 20, 23, 24, 27, 28, and 37 under 35 U.S.C. 102(b) as being anticipated by Gerdes et al (Proc. Natl. Acad. Sci.), Applicant submits that Gerdes et al (PNAS) disclose *E. coli* containing a hok gene which is expressed only when the temperature is raised to 42 degrees and the lambda CI857 is inactivated, and a sok gene regulated by the temperature-sensitive lambda CI857 repressor. Applicant asserts that the "sok gene is expressed only when the temperature is raised to 42 degrees C and the lambda CI857 is inactivated. Applicant submits that "the hok can be considered a lethal gene", and "the sok gene can be considered a regulatory gene". However, Applicant maintains that Gerdes et al fail to disclose any environmentally regulated "essential" gene.

However, it is the Examiner's position that if the sok gene is expressed only when the temperature is 42 degrees, it is considered to be environmentally regulated. Furthermore, since expression of the sok gene regulates expression of the hok gene

(the lethal gene), it would be considered "essential" as the sok gene suppresses killing by encoding a product which counteracts the hok-mediated killing by interfering with a vital function in the cell membrane. Therefore, the sok gene is considered "essential" to the viability of the cell.

(c) In response to the rejection of claims 1-3, 8, 10-14, 16, 20, 27, 28, and 37 under 35 U.S.C. 102(b) as being anticipated by Gerdes et al (EMBO Journal), Applicant submits that Gerdes et al disclose the hok gene, but the reference fails to disclose a temperature regulated sok gene. Applicant asserts that "Gerdes et al (EMBO) does not disclose any regulated form of the sok gene". Applicant also cites Franch and Gerdes (Molecular Microbiology 21:1049-1060, 1996) and asserts that the claimed Environmentally Limited Viability System is not intended to be a regulatory gene regulating expression of a lethal gene.

However, it is the Examiner's position that Gerdes et al disclose the sok (suppressor of killing) gene. Gerdes et al also disclose that the hok gene is activated at high temperature (41 degrees C), and the sok gene counteracts the hok gene. Therefore, the sok gene is considered "essential" to the viability of the cell.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to V. Ryan whose telephone number is (703)305-6558.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-0196.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027.

Papers related to this application may be submitted to the Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax number for Art Unit 1641 is (703)308-4242.

V. Ryan
Patent Examiner/Art Unit 1641
May 1998
Ryan/vr

James C. Housel 5/6/98

JAMES C. HOUSEL
SUPERVISORY PATENT EXAMINER